Graybug Vision Inc.

STATISTICAL ANALYSIS PLAN

Official Title: A Phase 2a Multicenter Study Evaluating the Safety, Tolerability, and Pharmacodynamics of a Single Injection of a Long-acting Intravitreal Sunitinib Malate Depot Formulation (GB-102) in Subjects with Diabetic Macular Edema (DME) and Retinal Vein Occlusion (RVO)

Protocol Number: GBV-102-003

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Sponsor: Graybug Vision, Inc.

Protocol Number: GBV-102-003

Author: [redacted]

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Statistical Analysis Plan Approval

Prepared by: [redacted]

Date

[redacted]

Reviewed by:

Date

[redacted]

Approved by:

Date

[redacted]

Approved by:

Date

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List of Abbreviations

ADL	Activities of Daily Living
AE	Adverse Event
AREDS	Age-Related Eye Disease Study
ATC	Anatomical Therapeutic Chemical
BCVA	Best Corrected Visual Acuity
CFP	Color Fundus Photography
CS	Clinically Significant
CST	Central Subfield Thickness
DME	Diabetic Macular Edema
DR	Diabetic Retinopathy
eCRF	Electronic Case Report Form
ETDRS	Early Treatment Diabetic Retinopathy Study
FAS	Full Analysis Set
ICH	International Council for Harmonisation
IOP	Intraocular Pressure
IVT	Intravitreal
MedDRA	Medical Dictionary for Regulatory Activities
NCI-CTCAE	National Cancer Institute – Common Terminology Criteria For Adverse Events
NCS	Not Clinically Significant
PP	Per Protocol
PT	Preferred Term
RVO	Retinal Vein Occlusion
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDC	Statistics & Data Corporation
SD-OCT	Spectral Domain – Optical Coherence Tomography
SOC	System Organ Class
SS	Safety Analysis Set
TEAE	Treatment-Emergent Adverse Event
VEGF	Vascular Endothelial Growth Factor
WHODrug	World Health Organization Drug Dictionary

1. Introduction

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and reporting for protocol GBV-102-003, version 2.0 dated 13 November 2019.

This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonization (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline, entitled Guidance for Industry: Structure and Content of Clinical Study Reports.

This SAP describes the data that will be analyzed and the subject characteristics, pharmacodynamics, and safety assessments that will be evaluated. This SAP provides details of the specific statistical methods that will be used. The statistical analysis methods presented in this document will supersede the statistical analysis methods described in the clinical protocol. If additional analyses are required to supplement the planned analyses described in this SAP they may be completed and identified in the clinical study report.

2. Study Objectives

Primary Objective:

To evaluate the safety and tolerability of a single intravitreal (IVT) injection of two different dose strengths of GB-102 (1 mg, 2 mg) in subjects with macular edema secondary to diabetic retinopathy (DR) or retinal vein occlusion (RVO) who have received prior induction with anti-vascular endothelial growth factor (VEGF).

Secondary Objective:

To evaluate the pharmacodynamic response as measured by best corrected visual acuity (BCVA) and central subfield thickness (CST) and time to first rescue injection.

3. Study Variables

Primary Endpoint

Safety

- Occurrence of ocular and non-ocular adverse events (AE) and serious adverse events (SAE) at all study visits

Secondary Endpoints

Pharmacodynamic Activity –

- BCVA (Early Treatment Diabetic Retinopathy Study [ETDRS] protocol) at all study visits
- CST (spectral-domain optical coherence tomography [SD-OCT]) at all study visits
- Observed subjects rescue-free at each study visit
- Time to first rescue injection
- Response to rescue treatment

Other Variables

- Slit-lamp biomicroscopy

- Dilated ophthalmoscopy
- Intraocular pressure (IOP)
- Physical examination
- Vital signs
- Color fundus photography (CFP)

4. Study Design and Procedures

4.1 General Study Design

This is a Phase 2a, multicenter, open-label, single injection, parallel arm, non-controlled safety, tolerability, and pharmacodynamics study. Eligible subjects will be enrolled to 1 of 2 concurrently initiated open-label GB-102 treatment arms: Group 1: 1 mg (50 µL) and Group 2: 2 mg (50 µL). Subjects will receive the IVT injection of the study drug in the study eye on Day 1.

The planned study assessments (AEs including SAEs, physical examinations, vital signs, BCVA using the ETDRS protocol, slit-lamp biomicroscopy findings, IOP measurements, dilated ophthalmoscopy results, and date of administration of rescue treatment) are conventional parameters used to evaluate the safety of pharmacologic agents in retinal disease. Approximately 20 subjects are planned: 10 subjects treated with 1 mg GB-102 and 10 subjects treated with 2 mg GB-102. There is no pre-set limitation on the proportion of diabetic macular edema (DME) or RVO subjects per dose group. Rescue treatment allowed is any anti-VEGF (aflibercept, bevacizumab, or ranibizumab) and should be used in accordance with the sites standard practice in administering these agents for the treatment of DME or RVO.

Pharmacodynamic activity will be assessed by means of BCVA (using the ETDRS Protocol), retinal CST using SD-OCT, and CFP (including wide field fundus photography, if available).

The null and alternative hypotheses, based on the primary variables, are as follows:

4.2 Schedule of Visits and Assessments

GB-102 will be administered on Day 1 in both Cohorts. Subjects will return to the study center on Days 14, 30, 60, 90, 120, 150, and 180 for safety and clinical assessments. Subjects will exit the study following all study assessments on Day 180.

The schedule of visits and assessments is provided in Table 1 below.

Table 1. Study Plan and Schedule of Assessments

Activity/Assessment	S[a]	B	W 2	M 1	M 2	M 3	M 4	M 5	M 6 (ET)
Visit Day ± Window[b]	**−30 to −3**	**1**	**14±2**	**30±4**	**60±7**	**90±7**	**120±7**	**150±7**	**180±7**
Informed Consent/HIPAA	X								
Inclusion/Exclusion Criteria	X								
Demographics Data	X								
Medical/Medication History	X								
Physical Examination	X								X
Pregnancy Testing[c]	X	X				X			X
Clinical Laboratory Tests[d]	X								
Adverse Events	X	X[e]	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X
Vital Signs[f]	X	X							X
BCVA (ETDRS)[g]	OU	OU	OU	OU	OU	OU	OU	OU	OU
Slit-lamp Biomicroscopy	OU	OU	OU	OU	OU	OU	OU	OU	OU
IOP[h]	OU	OU	OU	OU	OU	OU	OU	OU	OU
Dilated Ophthalmoscopy	OU	OU	OU	OU	OU	OU	OU	OU	OU
SD-OCT[i]	OU	OU	OU	OU	OU	OU	OU	OU	OU
Intravitreal Depot Photography[j]		SE	SE	SE	SE	SE	SE	SE	SE
GB-102 Injection[k]		SE							
Post-injection Assessment[l]		SE							
Follow-Up Call[e]		+1 day							

B = Baseline Visit; BCVA = Best Corrected Visual Acuity; ET = Early Termination; ETDRS = Early Treatment Diabetic Retinopathy Study; HIPAA = Health Insurance Portability and Accountability Act; IOP = Intraocular Pressure; M = Month; OU = Both Eyes; S = Screening Visit; SD-OCT = Spectral Domain-Optical Coherence Tomography; SE = Study Eye; V = Visit; W = Week

a Screening Visit to occur 3 to 30 days before study baseline (Day 1) to ensure that laboratory results are obtained. Imaging eligibility based on SD-OCT will be Investigator determined; there is no reading center confirmation.

b The protocol-specified procedures for a given study visit may be split across 2 days within the visit-specific window (if applicable); however, for each visit, all BCVA, ophthalmic examinations, and ophthalmic imaging must be performed on the same day and cannot be split across 2 or more days. Evaluations should be performed by the same evaluator for the same subject throughout the study whenever possible. If it is not possible to use the same evaluator to follow the subject, then evaluations should overlap (examine the subjects together and discuss findings) for at least 1 visit.

c Urine pregnancy test in women of childbearing potential only; additional pregnancy tests may be performed at any time/day during the study.

d Chemistry (non-fasting blood): hemoglobin A1c.

e All subjects will receive a telephone call for the day after the intravitreal injection to assess for any significant complaints or adverse events.

f Heart rate, blood pressure; additional collection of height (without shoes) will be measured at Screening and body weight will be measured at Screening and Month 6/exit.

g Visual acuity assessment using ETDRS protocol at 4 m with manifest refraction will be performed at all visits; 1 m may be performed if needed.

h Goldmann applanation tonometry or Tono-Pen acceptable; however, technique used at baseline must be used at all subsequent visits. Intraocular pressure will be checked before dilation and the IVT injection of study drug at dosing visits.

i Measurements for CST determined by the Investigator (no central reading center confirmation).

j Wide field color fundus photography (eg, Optos Ultra-widefield or Zeiss Clarus 500 or other ultra-widefield equipment) of the intravitreal GB-102 depot will be obtained following the dilated ophthalmic examination at all visits – if available at the study site. The initial images of the depot should be obtained at baseline (Day 1) ***after*** the IVT injection of GB-102 and conducted through (and include) the final study visit and any unscheduled visits. The photographs may be used to document the general appearance and rate of bioabsorbability of the depot. If no wide-FOV camera available, standard 30-degree field of view (FOV) imaging documenting the visual axis will be sufficient. For detailed instructions regarding collection of the intravitreal depot CFP imaging, refer to the separately provided guideline.

k Following intravitreal injection of GB-102, the subject should remain seated for approximately 15 minutes post-injection with minimal to no movement of the head (e.g., bending over, shaking head, laying down) and avoid significant eye movement.

l Postinjection assessment to consist of checking for count fingers or hand motion vision within 15 minutes after injection; if needed, subject can be examined (eg, additional IOP or ophthalmoscopy, per discretion of the Investigator) prior to going home.

4.3 Masking

This is an open-label study and the injecting investigator/physician may be the assessing investigator. The SD-OCT and CFP technicians and other site personnel, the Sponsor, and CRO are unmasked to treatment assignment.

5. Sample Size

The sample size is within clinical standards for the establishment of preliminary safety of GB-102. The sample size of this study was not selected to support specific statistical hypothesis testing. A sample size of approximately 20 evaluable subjects in the FAS analysis set allows for detection of adverse events with rates that exceed 15% overall and exceed 30% for each dose with approximately 95% confidence.

6. Data Preparation

All reported study data will be recorded on the electronic case report forms (eCRF) supplied by Statistics & Data Corporation (SDC) using iMedNet™. Only the Principal Investigator and authorized study staff according to the Delegation of Responsibilities log are entitled to make entries in the eCRF. After data is entered into the clinical study database, electronic edit checks, and data review will be performed. All data validation specifications and procedures are detailed in the Data Validation Manual as a separate document. When the database has been declared to be complete and accurate, the database will be locked. Any changes to the database after data have been locked can only be made with the approval of the Sponsor and Ora in consultation with SDC.

All analyses outlined in this document will be carried out after the following have occurred:

- All data management requirements are met according to SDC standard operating procedures, including data entry, performance of edit and validation checks, documentation, and resolution of

data queries and database lock with written authorization provided by appropriate SDC and Sponsor personnel.

- Protocol deviations have been identified and status defined (major/minor deviations).
- Analysis sets have been determined.

7. Analysis Sets

7.1 Safety Analysis Set

The safety analysis set (SS) includes all subjects who received a dose of study treatment. Subjects who receive rescue treatment during the study will be included in the SS. Subjects will be analyzed according to actual treatment received.

7.2 Full Analysis Set

The full analysis set (FAS) includes all subjects who received a dose of study treatment and complete a baseline and a post-baseline visit. Subjects will be analyzed according to the actual treatment they received.

7.3 Per Protocol

The per protocol (PP) analysis set consists of a subset of the FAS and includes subjects with no major protocol violations that would affect the assessment of the pharmacodynamics, and rescue data.

8. General Statistical Considerations

8.1 Unit of Analysis

The unit of analysis in this study will be the study eye for all safety and pharmacodynamic summaries. The study eye was selected as the eye that meets all the inclusion criteria and none of the exclusion criteria. If both eyes meet the inclusion and none of the exclusion criteria, the eye with the worst visual acuity at baseline will be selected. If both eyes have the same baseline visual acuity, the right eye will be selected as the study eye. Additionally, non-ocular AEs and medical history will be presented at the subject level. Non-study eye safety summaries will also be presented as appropriate.

8.2 Missing or Inconclusive Data Handling

In general, there will be no imputation of missing data other than for partial or missing dates where complete dates are required to flag data as treatment-emergent or concomitant with treatment. Partial/missing start and end dates for AEs and concomitant medications will be imputed as follows:

Partial/missing start date:

· Dates with missing day only will be imputed as the 1st of the month unless the month and year are same as the month and year of first dose of study medication, in which case missing day will be imputed as the first dose day of study medication.

· Dates with both day and month missing will be imputed as 1 Jan unless the year is same as the year of first dose of study medication, in which case missing day and month will be imputed as the first dose day and month of study medication.

· Completely missing dates will not be imputed.

Partial/missing end date:

· Dates with missing day only will be imputed as the last day of the month unless the month and year are the same as the month and year of the last dose of study medication, in which case missing day will be imputed as the last dose day of study medication.

· Dates with both day and month missing will be imputed as 31 Dec unless the year is same as the year of the last dose of study medication, in which case missing day and month will be imputed as the last dose day and month of study medication.

· If the ongoing flag is missing or “Yes” then the date will not be imputed unless death date is available, in which case the missing date will be imputed as the death date. If ongoing is “No” then the missing end date will be imputed as the last dose date.

The original dates will be displayed in data listings and the imputed dates will be used in derivations only (study day, treatment-emergence status, etc).

8.3 Definition of Baseline

Baseline is defined as the last measurement prior to the administration of study medication. Change from baseline will be calculated as post-baseline visit minus baseline visit.

8.4 Data Analysis Conventions

The final data analysis will be performed by SDC after the study is completed and the database has been locked. Statistical programming and analyses will be performed using SAS® Version 9.4 or higher. Output will be provided in rich text format (RTF) for tables and portable document format (PDF) for tables, listings, and figures using landscape orientation. All study data will be listed by subject, treatment, and visit (as applicable).

Summaries for continuous and ordinal variables will include the number of observations (n), arithmetic mean, standard deviation (SD), median, minimum, and maximum. Minima and maxima will be reported with the same precision as the raw values; means and medians will be presented to one additional decimal place than reported in the raw values. Standard deviations will be presented to two additional decimal places than reported in the raw values. Summaries for discrete variables will include number of observations, and percentages. All percentages will be rounded to one decimal place (i.e., XX.X%). Unless otherwise specified, summaries will be presented by cohort and, where appropriate, visit.

8.5 Adjustments for Multiplicity

No statistical adjustments for multiplicity are planned due to the exploratory nature of this study.

9. Disposition of Subjects

Subject disposition will be presented in terms of the numbers and percentages of subjects who completed the study and discontinued from the study. Subjects who are not discontinued from the study will be considered study completers. Disposition will be summarized by cohort and for total subjects. The number of subjects in each of the analysis sets (FAS, PP, and SS) will be displayed by cohort total subjects. Percentages will be calculated using enrolled subjects as the denominator.

The number and percentage of subjects enrolled, and failed screening will be presented using total number of subjects screened as denominator. Reasons for screen failures would include number and percentage of subjects who either failed to meet inclusion criteria or met exclusion criteria.

The number and percentage of subjects prematurely discontinued from the study and the reasons for study discontinuation will be summarized by cohort for all enrolled subjects. The reasons for study discontinuation that will be summarized include withdrawal of consent, lost to follow-up, adverse event, sponsor termination of study, and other. A subject listing will be provided that includes the date of and reason for premature study discontinuation.

The number and percentage of subjects with major protocol deviations will be summarized by cohort and total enrolled subjects. The protocol deviations that will be summarized include: informed consent, inclusion/exclusion or treatment assignment, test article/study drug administration at site, improper protocol procedures at site, site's failure to report SAE, visit out of window, subject's use of prohibited concomitant medication, subject's failure to follow instructions, and other. A subject listing will be provided that includes the start and end date of the deviation, the deviation code, the deviation description, and the classification of whether the deviation was judged to be major or minor.

In addition, subject listings will be provided that include informed consent date, inclusion and exclusion criteria violations, and exclusions from the Per Protocol Analysis Set.

10. Demographic Variables and Pretreatment Variables

10.1 Demographic Variables

The demographic variables collected in this study include age, sex, race, ethnicity, and iris color of study eye. Demographic variables will be summarized for the FAS, PP and Safety analysis sets, separately. Subjects who report more than one race will be summarized in the Multiple Race category. Age will also be categorized as follows: < 65 and ≥ 65 years. Age will be reported in years and calculated using the following formula:

Age = (Informed Consent Date - Date of Birth) / 365.25, truncated as an integer

The number and percentage of subjects will be presented, overall and by cohort, for age, sex, race, ethnicity, and iris color for the study eye.

A subject listing that includes all demographic variables will be provided.

10.2 Pretreatment Variables and Anti-VEGF History

Pretreatment variables will include baseline BCVA and CST in the study eye. Baseline BCVA, and baseline CST will be summarized, total and by cohort, using continuous descriptive statistics. Additionally, all two pretreatment variables will be categorized as follows: SD-OCT (≤350 and >350 micrometers), and BCVA (≤68 versus >68 letters).

Anti-VEGF history will include previous number of Anti-VEGF injections, time (in months) since first anti-VEGF and last anti-VEGF. Number of injections will be summarized as categorical variable (<5 versus ≥5) and time since first and last injections will be summarized as continuous variables. All the summaries will be presented, total and by cohort.

Subject listings including all pretreatment variables and Anti-VEGF history will be provided.

11. Medical History and Concomitant Medications

11.1 Medical History

Medical history will be coded using the medical dictionary for regulatory activities (MedDRA) version 22.0. Non-ocular medical history will be summarized using discrete summary statistics and presented by cohort at the subject and event level by System Organ Class (SOC) and Preferred Term (PT) using the SS. Ocular medical history will be similarly summarized at the subject level by study and non-study eye. If a subject reports the same PT multiple times within the same SOC, that PT will only be reported once within that SOC. As with the PT, if a subject reports multiple conditions within the same SOC, that SOC will only be reported once. SOCs and PTs will be listed in alphabetical order.

Listings of medical history will be generated separately for ocular and non-ocular data.

11.2 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHODrug) Global (B3, March 2019) and summarized to the therapeutic drug class (Anatomical Therapeutic Chemical [ATC] 4 classification) and preferred name. If the ATC 4 classification is not provided, the next lowest classification that is provided in the coding dictionary will be used. The preferred name will be defined as the active ingredient; if the active ingredient is not provided or includes more than two ingredients (e.g., multivitamins), then the drug name will be summarized as the preferred name. Any uncoded terms will be summarized under the ATC classification and preferred name of “Uncoded.” Prior medications are defined as those medications listed as having stopped prior to initiation of study drug. Concomitant medications are defined as those medications listed as having been taken: (1) prior to initiation of study drug and continuing for any period of time following the first administration of study drug, or (2) at

any time following the first administration of study drug. Prior medications are defined as medications initiated prior to study drug Administration including both those stopped before baseline and those continued after baseline.

Prior and Concomitant medications will be summarized for ocular and non-ocular medications separately using the SS. All the ocular events will also be further summarized by study and non-study eye. Medications will be tabulated for each cohort using frequencies and percentages. Subjects may have more than 1 medication per ATC text. At each level of subject summarization, a subject will be counted once if 1 or more medications is reported. Percentages will be based on the number of subjects in each cohort. ATC classes and preferred names within an ATC class are listed in alphabetical order.

Listings of prior and concomitant medications and procedures will be generated separately for ocular and non-ocular data.

11.3 Study Drug Administration

Descriptive summary statistics of study drug administration will be tabulated by each cohort. Variables like study eye (OD/OS), drug administration performed as per pharmacy manual (Yes/No), completion of post-injection assessment (Yes/no) will be included in the analysis.

A subject listing of study drug administration will be generated.

12. Pharmacodynamic Analysis

BCVA, CST (using SD-OCT), and rescue treatment (time to first rescue treatment, number of rescue treatments) will be included as pharmacodynamic endpoints. No formal hypothesis testing will be conducted. Descriptive summaries will include the arithmetic mean, SD, median, minimum, and maximum values for continuous variable, and the number of subjects and percentages for categorical variable.

Observed data will contain assessments performed during protocol defined and unscheduled visits including ones performed after the first rescue treatment. To allow for an efficacy assessment of GB-102 while excluding potential effects from rescue injections data collected after first rescue treatment will be censored and replaced with the last value collected prior to the first rescue treatment. The LOCF approach is used for the analysis of BCVA and CST.

Sensitivity analysis will also be conducted using observed data without any censoring and imputation as mentioned in the previous paragraph.

The response to anti-VEGF rescue treatment is assessed for BCVA and CST based on the data collected prior and after the first rescue treatment. This response analysis will include all subjects receiving at least one rescue treatment. The last assessment performed before receiving the first rescue treatment will be used as the rescue treatment related baseline value. Data from one month and two months prior to the rescue treatment - baseline as well as one and two months post rescue treatment will be used to assess

the response to rescue treatment. These five timepoints will represent the time-scale for these analyses. No imputation for missing data will be done.

Summaries will be produced for the overall as well as by diagnosis (DME or RVO) within FAS and PP analysis set.

All observed pharmacodynamic variables will also be presented by visit in subject listings.

12.1 BCVA

Visual acuity assessment (BCVA) using ETDRS protocol with manifest refraction will be performed in both eyes at all visits. The number of letters read correctly in the study eye will be the BCVA endpoint.

12.1.1 LOCF AND OBSERVED DATA APPROACH

Values and change from baseline in number of letters read correctly will be summarized using LOCF approach for study eye by visit and cohort using continuous descriptive statistics. Categorical change from baseline will also be summarized for study eye by visit, total and by cohort.

Observed values and change from baseline in number of letters read correctly will be summarized for study eye by visit and cohort using continuous descriptive statistics. Categorical changes from baseline will also be summarized for study eye by visit, total and by cohort.

12.1.2 RESPONSE TO FIRST RESCUE TREATMENT ANALYSIS

For the subset of subjects with at least one rescue treatment the observed and change from rescue treatment baseline in number of letters read correctly will be summarized for study eye by time-point and cohort using continuous descriptive statistics.

12.2 CST (spectral-domain optical coherence tomography [SD-OCT])

The SD-OCT imaging will be performed for both eyes to measure and assess cross-sectional images of the anatomic layers of the retina and to detect the presence of retinal fluid. Images will be obtained using a SD-OCT device by designated certified study center personnel. Preferably the same device will be used for screening and the subsequent follow-up assessments for each subject. Images will be read centrally, and CST measurement data provided to SDC.

12.2.1 LAST OBSERVATION CARRIED FORWARD AND OBSERVED DATA APPROACH

Values and change from baseline in CST measurements will be summarized using LOCF approach for study eye by visit and cohort using continuous descriptive statistics. Categorical change from baseline will also be summarized for study eye by visit, total and by cohort.

Observed values and change from baseline in CST measurements will be summarized for study eye by visit and cohort using continuous. Categorical changes from baseline will also be summarized for study eye by visit, total and by cohort.

12.2.2 RESPONSE TO FIRST RESCUE TREATMENT ANALYSIS

For the subset of subjects with at least one rescue treatment the observed and change from rescue treatment baseline in number of letters read correctly will be summarized for study eye by time-point and cohort using continuous descriptive statistics.

12.3 Rescue-free treatment

Rescue treatment (any anti-VEGF agent; aflibercept, bevacizumab, or ranibizumab) for all subjects enrolled is allowed at any visit following the Day 30 study assessments in subjects who meet any of the following criteria regarding decrease in BCVA and/or increase in CST:

Decrease in BCVA:

- ≥ 10 ETDRS letter decrease compared with best on-study (i.e., post-treatment) BCVA ETDRS letter score

Increase in CST (any of the following criteria)

- ≥ 75 µm compared with the average of the last 2 on-study (i.e., post-treatment) visit CST measurements (µm), and/or,
- ≥ 100 µm compared with the lowest on-study (i.e., post-treatment) CST measurement (µm)

Subjects may receive rescue treatment during a scheduled or unscheduled visit. Rescue treatment received during an unscheduled visit will be counted towards next scheduled visit.

Time to first rescue treatment including median time to first rescue treatment will be assessed using Kaplan-Meier product-limit approach by cohort. Subjects will be considered to have an event at the date where rescue treatment for study eye was first initiated. Since rescue treatment may be initiated at any time – at a scheduled visit or between scheduled visits – the timing of rescue treatment usage will be based on the date in at which rescue treatment was started. Subjects who do not have any usage of rescue treatment in the study eye will be censored at the date of the last visit. Subjects who discontinue prior to completing all treatment period visits will be evaluated based on the visits which are available. Kaplan-Meier plots will be generated.

For the subgroup of subjects with rescue treatment the time to first rescue treatment will be summarized by cohort using continuous descriptive statistics.

Proportion of subjects receiving rescue treatment during any protocol defined visit will be tabulated by cohort. As subjects will be eligible to receive rescue treatment on or after Day 30, Month 1 will be the first visit to be included in this table.

A contingency table will be generated to represent a cross-classification between whether rescue criteria were met (yes or no) versus received rescue treatment (yes or no). Contingency will be checked across all visits as well as at every visit starting from Month 1.

The total number of rescue treatments received by each subject will be tabulated.

Rescue treatment will be listed by subject and medication.

13. Safety Analyses

All safety analyses will be conducted using the SS.

13.1 Adverse Events

An adverse event (AE) is defined as any untoward medical occurrence associated with the use of a drug in humans, whether it is considered drug related. An AE can therefore be any unfavorable and unintended medical diagnosis, sign, or symptom; any new undesirable medical occurrence or unfavorable or unintended change in a pre-existing condition that occurs during or after study treatment; or laboratory abnormality, vital sign, or ophthalmic assessment that is assessed as clinically significant and different from baseline (e.g., requiring discontinuation of study treatment, specific treatment, or a change in subject management). If possible, changes in laboratory results or changes in vital signs that meet the definition of an AE should be reported as a medical diagnosis rather than as the abnormal value. All AEs will be coded using MedDRA Version 22.0.

A treatment-emergent adverse event (TEAE) is an AE with an onset anytime from when the subject has received study drug through 30 days after the study ends whether it is considered causally related to the study drug. Adverse events recorded in the eCRF which began prior to treatment will not be included in the summary tables but will be included in the AE data listings. An SAE is any event that involves or results in any of the following outcomes:

- Death
- Life-threatening occurrence (i.e., if in the view of the investigator or Sponsor, the event's occurrence placed the subject at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
- Requires in-patient hospitalization or prolongation of existing hospitalization (hospitalization for elective surgery for a pre-existing condition or for surgery planned before study entry is not considered an SAE)
- A persistent or significant disability/incapacity (permanent or substantial disruption of the subject's ability to perform normal life functions); this definition is not intended to include experiences of relatively minor or temporary medical significance
- Congenital anomaly/birth defect (an AE that occurs in the child or fetus of a subject exposed to study drug prior to conception or during pregnancy)
- An important medical event or serious medical condition that does not meet any of the above criteria may be considered an SAE if, based upon appropriate medical judgment, it jeopardizes the subject or requires medical or surgical intervention to prevent one of the outcomes listed above. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias, or convulsions that do not result in in-patient hospitalization, or the development of drug dependency or drug abuse.

An overall summary will be presented that includes the number of TEAEs and the number and percentage of subjects who experienced at least one TEAE, total and by cohort. This summary will also include breakdowns of TEAEs further categorized as ocular (study eye and non-study eye, separately), non-ocular, serious TEAEs, TEAEs by maximum severity, treatment-related TEAEs, and TEAEs leading to subject withdrawal.

Additional summaries of TEAEs will be provided showing the number and percentage of subjects who experienced at least one TEAE and total number of events. These summaries will be presented by SOC and PT. Non-ocular TEAEs will be summarized using discrete summary statistics and presented by cohort and total subjects at the subject and event level by SOC and PT. Ocular TEAEs will be similarly summarized at the subject level for study and non-study eyes separately. If a subject has multiple TEAEs coded to the same PT within same SOC, that PT will only be reported once. As with the PT, if a subject reports multiple conditions within the same SOC, that SOC will only be reported once at the subject level. In the summary, SOCs are listed in order of decreasing frequency for total subjects. PTs are listed in order of decreasing frequency within each SOC for total subjects. The occurrence of non-ocular and ocular TEAEs will also be tabulated by SOC and PT for the following: maximal severity and suspected relationship to study drug.

Separate summaries will be provided for the following categories of AEs:

- Ocular TEAEs in the study eye
- Ocular TEAEs in the non-study eye
- Non-ocular TEAEs
- Treatment-related ocular TEAEs in the study eye
- Treatment-related ocular TEAEs in the non-study eye
- Treatment-related non-ocular TEAEs
- Ocular serious TEAEs in the study eye
- Ocular Serious TEAEs in the non-study eye
- Non-ocular serious TEAEs
- Treatment-related ocular serious TEAEs in the study eye
- Treatment-related ocular serious TEAEs in the non-study eye
- Treatment-related non-ocular TEAEs
- Ocular TEAEs by maximal severity in the study eye
- Ocular TEAEs by maximal severity in the non-study eye
- Non-ocular TEAEs by maximal severity
- TEAEs leading to premature study discontinuation (if applicable)

The NCI-CTCAE (National Cancer Institute – Common Terminology Criteria for Adverse Events) (version 4.03) is a descriptive terminology that will be used to grade the severity of non-ocular AEs reported in this

study. The NCI-CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observation only; intervention not indicated

Grade 2: Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL)*

Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limited self-care ADL**

Grade 4: Life-threatening consequences; urgent intervention indicated

Grade 5: Death related to an AE

A semicolon indicates "or" within the above descriptions. A single dash (-) can be used to indicate that a grade is not available. Not all grades are appropriate for all AEs. Therefore, some AEs are listed with fewer than 5 options for grade selection.

* Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

** Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not being bedridden.

The severity grading of ocular AEs reported in this study will not employ the NCI-CTCAE criteria defined above but will be graded as described here. Severity of an ocular AE is defined as a qualitative assessment of the degree of intensity of an AE as determined by the Investigator or reported to him/her by the subject. The assessment of severity is made irrespective of relationship to the study drug or seriousness of the event and should be evaluated according to the following scale:

- *Mild*: Event is noticeable to the subject but is easily tolerated and does not interfere with the subject's daily activities.
- *Moderate*: Event is bothersome, possibly requiring additional therapy, and may interfere with the subject's daily activities.
- *Severe:* Event is intolerable, necessitates additional therapy or alteration of therapy, and interferes with the subject's daily activities.

Summaries of TEAEs by maximal severity will be provided showing the number and percentage of subjects who experienced at least one TEAE and total number of events. These summaries will be presented by SOC and PT. Non-ocular TEAEs will be summarized using discrete summary statistics and presented by cohort and total subjects at the subject and event level by SOC and PT. Ocular TEAEs will be similarly summarized at the subject level for study and non-study eyes separately.

The relationship of each AE to the study drug should be determined by the Investigator using these explanations:

- *Related*: A reasonable possibility exists that the study drug caused the AE.
- *Not Related*: A reasonable possibility does not exist that the study drug caused the AE.

Summaries of all ocular and non-ocular TEAEs, TEAEs by maximal severity, TEAES related to the study drug, and serious TEAEs will also be tabulated by study site for each cohort and total subjects. All ocular AEs occurred in study eye and non-study eye will be summarized separately.

All TEAEs will be presented in a subject listing. The TEAEs leading to study treatment discontinuation will be listed separately. In addition, all serious AEs will be presented in a separate listing.

13.2 BCVA (ETDRS)

The observed and change from baseline BCVA letter score will be summarized for the study eye and non-study eye using continuous descriptive statistics by visit for each cohort and for all subjects combined. A subject listing of visual acuity will also be produced. This listing will include a variable that indicates if a subject had a visual acuity worsening from baseline of ≥10 letters.

13.3 Slit-Lamp Biomicroscopy Examination

A slit-lamp biomicroscopy examination of the eyelid, cornea, conjunctiva, anterior chamber, iris, pupil, lens, lens status, and Age-Related Eye Disease Study (AREDS) scores for Nuclear, Cortical, and PCS opacity will be performed at each visit. The results will be graded as normal, abnormal not clinically significant (NCS), or abnormal clinically significant (CS) for all but the lens status and AREDS scores. Lens status will be denoted phakic, pseudophakic, or aphakic. AREDS opacity scores are <1, 1, 1.5, 2, 2.5, 3, or >3. Anterior chamber cells and flare will also be assessed using categorical responses that range from 0 to 4+, as described below.

Anterior Chamber Cells:

Grade	Number of cells
0	None
+0.5	1 – 5
+1	6 - 15
+2	16 – 25
+3	26 – 50
+4	> 50

Anterior Chamber Flare:

Grade	Description
0	None
+1	Trace
+2	Moderate (iris and lens detail clear)

+3 Marked (iris and lens detail hazy)

+4 Intense (fibrin or plastic aqueous)

The results will be summarized using counts and percentages for each cohort and for all GB-102 treated subjects combined at each visit for each eye (study eye and non-study eye). Percentages will be based on the number of subjects in each cohort with responses. Shift tables for each biomicroscopy parameter will also be provided comparing each follow-up visit to baseline. A subject listing of the slit-lamp biomicroscopy parameters will also be produced.

13.4 Dilated Ophthalmoscopy

A dilated fundus examination of the vitreous, macula, peripheral retina, choroid, and optic nerve will be performed at each visit. The results will be graded as normal, abnormal NCS, or abnormal CS. The results will be summarized using counts and percentages for each cohort and for all subjects at each visit for each eye (study eye and non-study eye). Percentages will be based on the number of subjects in each cohort with responses. A shift table for the dilated ophthalmoscopy parameters will also be provided comparing each follow-up visit to baseline. A subject listing of the dilated ophthalmoscopy parameters will also be produced.

13.5 Intraocular Pressure (IOP)

Intraocular pressure (IOP) will be assessed using Goldmann applanation tonometry or Tono-Pen at each visit. Results will be taken from a single measurement and will be recorded in mmHg. Clinically relevant change in IOP indicates increase from baseline is at least 10 mmHg and absolute value is at least 25 mmHg at a visit. The IOP values, changes from baseline, and clinically relevant change for each eye (study eye and non-study eye) will be summarized using continuous descriptive statistics by visit and eye for each cohort and for all subjects combined. A subject listing of IOP will also be produced.

13.6 Physical Examination

The physical examination will consist of, at a minimum, a routine evaluation of the organ systems including general appearance, neck, head, ears, nose, throat, cardiovascular, respiratory, abdomen, and skin/extremities. At the final study visit, the physical examination will include a query of the subject to determine if changes in his/her physical condition have occurred since the screening examination. A subject listing of the physical examination results will be produced.

13.7 Vital Signs

Vital signs, including height, heart rate (HR) and systolic and diastolic blood pressure will be measured at Screening, Day 1, and Month 6. Body weight will be measured at Screening and Month 6. Height will be measured only at Screening. Changes from baseline will be summarized at Month 6 for applicable parameters. A subject listing of the vital signs results will also be produced.

13.8 Blood Chemistry

Blood samples for Hemoglobin A1c (nonfasting) will be collected prior to administration of study drug. Screening laboratory tests may be repeated once at the discretion of the Investigator. A subject listing of the blood chemistry results will be produced.

13.9 Pregnancy Testing

Urine pregnancy test will be conducted on women of childbearing potential as appropriate. Women of childbearing potential (i.e., not postmenopausal for at least 12 months or not surgically sterile [bilateral tubal ligation, hysterectomy, or bilateral oophorectomy]) must have a negative urine pregnancy test at Screening and must use adequate birth control throughout the study if she has a nonsurgically sterile male sexual partner. A subject listing of urine pregnancy test results will be produced.

14. Interim Analyses

Once all subjects complete the 3-month visit, an interim analysis (IA) will be performed on safety data. No statistical adjustments will be made for this exploratory study and due to the analysis being limited to safety endpoints and due to the absence of any hypothesis testing.

15. Tables

Tables that will be included in the topline delivery are shown in boldface italics font.

Table Number	Title	POPULATION
Table 14.1.1.1	***Subject Disposition***	***All Enrolled Subjects***
Table 14.1.1.2	Subject Enrollment Status	All Subjects Including Screen Failures
Table 14.1.2.1	***Demographic and Pretreatment Variables in Study Eye***	***Full Analysis Set***
Table 14.1.2.2	Demographic and Pretreatment Variables in Study Eye	Safety Analysis Set
Table 14.1.2.3	Demographic and Pretreatment Variables in Study Eye	Per Protocol Analysis Set
Table 14.1.4.1	Ocular Medical History	Safety Analysis Set
Table 14.1.4.2	Non-Ocular Medical History	Safety Analysis Set
Table 14.1.5.1	Ocular Prior Medications	Safety Analysis Set
Table 14.1.5.2	Ocular Concomitant Medications	Safety Analysis Set
Table 14.1.5.3	Non-Ocular Prior Medications	Safety Analysis Set
Table 14.1.5.4	Non-Ocular Concomitant Medications	Safety Analysis Set
Table 14.1.6	Study Drug Administration	Safety Analysis Set
Table 14.2.1.1	***Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits***	***Full Analysis Set – As Observed (Including Rescue Treatment)***
Table 14.2.1.2	Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits	Per Protocol Analysis Set – As Observed (Including Rescue Treatment)
Table 14.2.1.3	Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits by Diagnosis	Full Analysis Set – As Observed (Including Rescue Treatment)
Table 14.2.1.4	Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits by Diagnosis	Per Protocol Analysis Set – As Observed (Including Rescue Treatment)
Table 14.2.1.5	***Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits***	***Full Analysis Set – LOCF With Censoring For Rescue[1]***

Table 14.2.1.6	Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits	Per Protocol Analysis Set – LOCF With Censoring For Rescue[1]
Table 14.2.1.7	Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits by Diagnosis	Full Analysis Set – LOCF With Censoring For Rescue[1]
Table 14.2.1.8	Change from Baseline in Number of Letters Read Correctly (using BCVA) in the Study Eye at Scheduled Visits by Diagnosis	Per Protocol Analysis Set – LOCF With Censoring For Rescue[1]
Table 14.2.2.1	***Change from Baseline in Retinal CST (Using SD-OCT*** in µm***) in the Study Eye at Scheduled Visits***	***Full Analysis Set – As Observed (Including Rescue Treatment)***
Table 14.2.2.2	Change from Baseline in Retinal CST (Using SD-OCT in µm) in the Study Eye at Scheduled Visits	Per Protocol Analysis Set – As Observed (Including Rescue Treatment)
Table 14.2.2.3	Change from Baseline in Retinal CST (Using SD-OCT in µm) in the Study Eye at Scheduled Visits by Diagnosis	Full Analysis Set – As Observed (Including Rescue Treatment)
Table 14.2.2.4	Change from Baseline in Retinal CST (Using SD-OCT in µm) in the Study Eye at Scheduled Visits by Diagnosis	Per Protocol Analysis Set – As Observed (Including Rescue Treatment)
Table 14.2.2.5	***Change from Baseline in Retinal CST (Using SD-OCT*** in µm***) in the Study Eye at Scheduled Visits***	***Full Analysis Set – LOCF With Censoring For Rescue[1]***
Table 14.2.2.6	Change from Baseline in Retinal CST (Using SD-OCT in µm) in the Study Eye at Scheduled Visits	Per Protocol Analysis Set – LOCF With Censoring For Rescue[1]
Table 14.2.2.7	Change from Baseline in Retinal CST (Using SD-OCT in µm) in the Study Eye at Scheduled Visits by Diagnosis	Full Analysis Set – LOCF With Censoring For Rescue[1]
Table 14.2.2.8	Change from Baseline in Retinal CST (Using SD-OCT in µm) in the Study Eye at Scheduled Visits by Diagnosis	Per Protocol Analysis Set – LOCF With Censoring For Rescue[1]
Table 14.2.3.1	***Time to Receipt of Rescue Treatment Using Kaplan-Meier Approach***	***Full Analysis Set***
Table 14.2.3.2	Time to Receipt of Rescue Treatment Using Kaplan-Meier Approach	Per Protocol Analysis Set
Table 14.2.3.3	Time to Receipt of Rescue Treatment Using Kaplan-Meier Approach by Diagnosis	Full Analysis Set
Table 14.2.3.4	Time to Receipt of Rescue Treatment Using Kaplan-Meier Approach by Diagnosis	Per Protocol Analysis Set

Table 14.2.3.5	Mean Time to Receipt of First Rescue Treatment Among Rescued Subjects	Full Analysis Set
Table 14.2.3.6	Mean Time to Receipt of First Rescue Treatment Among Rescued Subjects	Per Protocol Analysis Set
Table 14.2.3.7	Mean Time to Receipt of First Rescue Treatment Among Rescued Subjects by Diagnosis	Full Analysis Set
Table 14.2.3.8	Mean Time to Receipt of First Rescue Treatment Among Rescued Subjects by Diagnosis	Per Protocol Analysis Set
Table 14.2.4.1	***Proportion of Subjects Receiving Rescue Treatment by Visit***	***Full Analysis Set***
Table 14.2.4.2	Proportion of Subjects Receiving Rescue Treatment by Visit	Per Protocol Analysis Set
Table 14.2.4.3	Proportion of Subjects Receiving Rescue Treatment by Visit, and Diagnosis	Full Analysis Set
Table 14.2.4.4	Proportion of Subjects Receiving Rescue Treatment by Visit, and Diagnosis	Per Protocol Analysis Set
Table 14.2.4.5	Contingency Table Showing Proportion of Subjects Receiving Rescue Treatment and Meeting Treatment Criteria by Visit	Full Analysis Set
Table 14.2.4.6	Contingency Table Showing Proportion of Subjects Receiving Rescue Treatment and Meeting Treatment Criteria by Visit	Per Protocol Analysis Set
Table 14.2.4.7	Contingency Table Showing Proportion of Subjects Receiving Rescue Treatment and Meeting Treatment Criteria by Visit, and Diagnosis	Full Analysis Set
Table 14.2.4.8	Contingency Table Showing Proportion of Subjects Receiving Rescue Treatment and Meeting Treatment Criteria by Visit, and Diagnosis	Per Protocol Analysis Set
Table 14.2.5.1	Total Number of Rescue Treatments Received by Each Subject	Full Analysis Set
Table 14.2.5.2	Total Number of Rescue Treatments Received by Each Subject	Per Protocol Analysis Set
Table 14.2.5.3	Total Number of Rescue Treatments Received by Each Subject, and Diagnosis	Full Analysis Set
Table 14.2.5.4	Total Number of Rescue Treatments Received by Each Subject, and Diagnosis	Per Protocol Analysis Set
Table 14.2.6.1	Time in the Study From First Rescue Treatment Received by Each Subject	Full Analysis Set

Table 14.2.6.2	Time in the Study From First Rescue Treatment Received by Each Subject	Per Protocol Analysis Set
Table 14.2.6.3	Time in the Study From First Rescue Treatment Received by Each Subject, and Diagnosis	Full Analysis Set
Table 14.2.6.4	Time in the Study From First Rescue Treatment Received by Each Subject, and Diagnosis	Per Protocol Analysis Set
Table 14.2.8.1	Change in Number of Letters Read Correctly (Using BCVA) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye	Full Analysis Set with a Rescue Treatment – As Observed
Table 14.2.8.2	Change in Number of Letters Read Correctly (Using BCVA) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye	Per Protocol Analysis Set with a Rescue Treatment – As Observed
Table 14.2.8.3	Change in Number of Letters Read Correctly (Using BCVA) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye, by Diagnosis	Full Analysis Set with a Rescue Treatment – As Observed
Table 14.2.8.4	Change in Number of Letters Read Correctly (Using BCVA) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye by Diagnosis	Per Protocol Analysis Set with a Rescue Treatment – As Observed
Table 14.2.9.1	Change in Retinal CST (Using SD-OCT in µm) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye	Full Analysis Set with a Rescue Treatment – As Observed
Table 14.2.9.2	Change in Retinal CST (Using SD-OCT in µm) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye	Per Protocol Analysis Set with a Rescue Treatment – As Observed
Table 14.2.9.3	Change in Retinal CST (Using SD-OCT in µm) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye by Diagnosis	Full Analysis Set with a Rescue Treatment – As Observed
Table 14.2.9.4	Change in Retinal CST (Using SD-OCT in µm) in Response to Anti-VEGF Rescue Treatment at Scheduled Visits in the Study Eye by Diagnosis	Per Protocol Analysis Set with a Rescue Treatment – As Observed
Table 14.3.1.1	***Overall Summary of Adverse Event***	***Safety Analysis Set***
Table 14.3.2.1	***All Ocular Treatment-Emergent Adverse Events in the Study Eye***	***Safety Analysis Set***
Table 14.3.2.2	All Ocular Treatment-Emergent Adverse Events in the Non-Study Eye	Safety Analysis Set
Table 14.3.2.3	All Non-Ocular Treatment-Emergent Adverse Events	Safety Analysis Set
Table 14.3.3.1	All Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product in the Study Eye	Safety Analysis Set

Table 14.3.3.2	All Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product in the Non-Study Eye	Safety Analysis Set
Table 14.3.3.3	All Non-Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product	Safety Analysis Set
Table 14.3.4.1	***All Ocular Treatment-Emergent Serious Adverse Events in the Study Eye***	***Safety Analysis Set***
Table 14.3.4.2	All Ocular Treatment-Emergent Serious Adverse Events in the Non-Study Eye	Safety Analysis Set
Table 14.3.4.3	***All Non-Ocular Treatment-Emergent Serious Adverse Events***	***Safety Analysis Set***
Table 14.3.5.1	All Serious Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product in the Study Eye	Safety Analysis Set
Table 14.3.5.2	All Serious Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product in the Non-Study Eye	Safety Analysis Set
Table 14.3.5.3	All Serious Non-Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product	Safety Analysis Set
Table 14.3.6.1	Incidence of Ocular Treatment-Emergent Adverse Events in the Study Eye by Maximum Severity, System Organ Class and Preferred Term	Safety Analysis Set
Table 14.3.6.2	Incidence of Ocular Treatment-Emergent Adverse Events in the Non-Study Eye by Maximum Severity, System Organ Class and Preferred Term	Safety Analysis Set
Table 14.3.6.3	Incidence of Non-Ocular Treatment-Emergent Adverse Events by Maximum Severity, System Organ Class and Preferred Term	Safety Analysis Set
Table 14.3.7	All Treatment-Emergent Adverse Events Leading to Premature Study Discontinuation	Safety Analysis Set
Table 14.3.8	Best Corrected Visual Acuity (BCVA) In Letters (ETDRS)	Safety Analysis Set
Table 14.3.9.1	Slit-Lamp Biomicroscopy	Safety Analysis Set
Table 14.3.9.2	Shifts in Slit-Lamp Biomicroscopy from Baseline to Each Post-Baseline Visit: Normal/Abnormal Responses	Safety Analysis Set
Table 14.3.9.3	Shifts in Slit-Lamp Biomicroscopy from Baseline to Each Post-Baseline Visit: AREDS Scores and Anterior Chamber Cells and Flare	Safety Analysis Set
Table 14.3.10.1	Dilated Ophthalmoscopy	Safety Analysis Set

Table 14.3.10.2	Shifts in Dilated Ophthalmoscopy from Baseline to Each Post-Baseline Visit	Safety Analysis Set
Table 14.3.11	Intraocular Pressure	Safety Analysis Set
Table 14.3.12	Vital Signs	Safety Analysis Set
Table 14.3.13.1	All Ocular Treatment-Emergent Adverse Events in the Study Eye by Site	Safety Analysis Set
Table 14.3.13.2	All Ocular Treatment-Emergent Adverse Events in the Non-Study Eye by Site	Safety Analysis Set
Table 14.3.13.3	All Non-Ocular Treatment-Emergent Adverse Events by Site	Safety Analysis Set
Table 14.3.14.1	Incidence of Ocular Treatment-Emergent Adverse Events in the Study Eye by Maximum Severity, System Organ Class,Preferred Term, and Site	Safety Analysis Set
Table 14.3.14.2	Incidence of Ocular Treatment-Emergent Adverse Events in the Non-Study Eye by Maximum Severity, System Organ Class,Preferred Term, and Site	Safety Analysis Set
Table 14.3.14.3	Incidence of Non-Ocular Treatment-Emergent Adverse Events by Maximum Severity, System Organ Class, Preferred Term, and Site	Safety Analysis Set
Table 14.3.15.1	All Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product in the Study Eye by Site	Safety Analysis Set
Table 14.3.15.2	All Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product in the Non-Study Eye by Site	Safety Analysis Set
Table 14.3.15.3	All Non-Ocular Treatment-Emergent Adverse Events Suspected to be Related to Investigational Product by Site	Safety Analysis Set
Table 14.3.16.1	All Ocular Treatment-Emergent Serious Adverse Events in the Study Eye by Site	Safety Analysis Set
Table 14.3.16.2	All Ocular Treatment-Emergent Serious Adverse Events in the Non-Study Eye by Site	Safety Analysis Set
Table 14.3.16.3	All Non-Ocular Treatment-Emergent Serious Adverse Events by Site	Safety Analysis Set

16. Listings

Listing Number	Title	Population
Listing 16.2.1	Subject Disposition	All Enrolled and Screen Failed Subjects
Listing 16.2.2.1	Major Protocol Deviations	All Enrolled Subjects
Listing 16.2.2.2	Inclusion/Exclusion Criteria Assessed by Investigator	All Enrolled and Screen Failed Subjects
Listing 16.2.3	Subjects Excluded from the Analysis Sets Per Protocol Population	All Enrolled Subjects
Listing 16.2.4.1	Demographics Variables	All Enrolled Subjects
Listing 16.2.4.2	Anti-VEGF History	All Enrolled Subjects
Listing 16.2.4.3	Baseline Disease Characteristics	All Enrolled Subjects
Listing 16.2.4.4	Ocular Medical History	All Enrolled Subjects
Listing 16.2.4.5	Non-Ocular Medical History	All Enrolled Subjects
Listing 16.2.4.6	Ocular Prior and Concomitant Medications	All Enrolled Subjects
Listing 16.2.4.7	Non-Ocular Prior and Concomitant Medications	All Enrolled Subjects
Listing 16.2.4.8	Prior Anti-VEGF Medications	All Enrolled Subjects
Listing 16.2.4.9	Concomitant Anti-VEGF Medications	All Enrolled Subjects
Listing 16.2.4.10	Ocular and Non-Ocular Prior and Concomitant Procedures	All Enrolled Subjects
Listing 16.2.4.11	Study Drug Administration	Safety Analysis Set
Listing 16.2.6.1	Retinal Central Subfield Thickness (CST) Using Spectral Domain Optical Coherence Tomography (SD-OCT in µm)	All Enrolled Subjects
Listing 16.2.7.1	All Adverse Events	Safety Analysis Set
Listing 16.2.7.2	Treatment Emergent Serious Adverse Events	Safety Analysis Set
Listing 16.2.7.3	Treatment-Emergent Adverse Events Leading to Premature Study Discontinuation	Safety Analysis Set
Listing 16.2.8.1	Best Corrected Visual Acuity (BCVA) Scores	All Enrolled Subjects
Listing 16.2.8.2	Slit Lamp Biomicroscopy	All Enrolled Subjects
Listing 16.2.8.3	Dilated Ophthalmoscopy	All Enrolled Subjects

Listing Number	Title	Population
Listing 16.2.8.4	Intraocular Pressure (IOP)	All Enrolled Subjects
Listing 16.2.8.5	Physical Examination	All Enrolled Subjects
Listing 16.2.8.6	Vital Signs	All Enrolled Subjects
Listing 16.2.8.7	Blood Chemistry	All Enrolled Subjects
Listing 16.2.8.8	Urine Pregnancy Test Results	All Enrolled Female Subjects

17. Figures

Figure Number	Title	Population
Figure 14.2.2.1	Kaplan Meier Curves of Time to Receipt of Rescue treatment	Full Analysis Set
Figure 14.2.2.2	Kaplan Meier Curves of Time to Receipt of Rescue treatment, Diagnosis = DME	Full Analysis Set
Figure 14.2.2.3	Kaplan Meier Curves of Time to Receipt of Rescue treatment, Diagnosis = RVO	Full Analysis Set